

CASE 7

A.A. (No. 8370-33), a male, aged 24, came to the clinic on July 12, 1933, complaining of swollen and painful knees and elbows, and pain in the shoulders and fingers.

Definite swelling and crepitations were found in both knees; the elbows were stiff and sore. Vaccine therapy was started on July 14, 1933. The dose that gave relief was found on about the eighth injection.

He had diseased tonsils. These were removed on January 12, 1934.

The genito-urinary report was negative. The Wassermann test was negative. Teeth, negative. The Ophthalmology Department reported on refraction. All the pains in all joints, except the knees, disappeared two months ago. Now the only condition which is retarding progress is fat-fringes, which are to be removed.

This patient is still disabled and walks with his knees somewhat flexed; they cannot be

extended. There is fullness below the patellæ, and pressure here brings on his pain.

For a trial of the vaccine three things are necessary:—

1. The vaccine.
2. Crowe's Handbook, which has to be followed closely.
3. A laboratory where the very concentrated vaccine, as received from England, may be diluted.

We have been very deeply indebted in this work to the other Departments of the Montreal General Hospital. They have investigated, prepared our vaccine, and treated many of our cases and have given us the most invaluable cooperation. Our thanks are heartily tendered to them.

HICCUP*

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THE recognition of hiccup, or singultus, by the ancients presents a historical background which dates back to the time of Hippocrates.¹ Their idea of its prognosis may be judged from the following quotations from his "Aphorisms", Libri V, VI, VII, "a convulsion or singultus supervening on excessive purging is a bad sign"; "Singultus and red eyes following vomiting are a bad sign"; "Either vomiting or singultus, or convulsions or delirium following ileus is a bad sign"; and finally "Singultus from inflammation of the liver is a bad sign". Reference is made to its treatment in the "Symposium" in the Dialogues of Plato as follows: Eryximachus, speaking to Aristophanes who is suffering from singultus during dinner, says, "Let me advise you to hold your breath, and if this fails then to gargle with a little water, and if the hiccup still continues tickle your nose with something and sneeze, and if you sneeze once or twice even the most violent hiccup is sure to go."¹ One could quote many ancient references to hiccup, its causation and treatment, but these will suffice to show that the early physicians appreciated something of its importance and attempted its cure.

Hiccup is caused by single or repeated clonic spasms of the diaphragm, with closure of the

glottis. Ordinarily, on inspiration, abduction of the glottis and vocal cords is synchronized with the muscles of respiration so that breathing is a noiseless act. In order to better understand the varied etiology of hiccup a brief review of the physiology of respiration is indicated. The diaphragm is innervated by the phrenic nerves on each side which arise in the neck chiefly from the 4th cervical segment, but also receives filaments from the 3rd, 5th and 6th. In its route to its distribution on the under surface of the diaphragm each nerve is in close relationship to the deep musculature of the neck, the first portion of the subclavian artery, subclavian vein, internal mammary artery, the root of the lung, and the pericardium. The left nerve is also in relationship to the left vagus and the arch of the aorta. In addition to their main function of supplying the diaphragm, all the nerves send filaments to the pleura and pericardium, and probably also to the peritoneum. There is also communication with the sympathetic system in the chest.² An accessory phrenic nerve is described by Alexander,³ occurring in 20 to 30 per cent of cases.

Control of respiration, as you are aware, is of a complex nature, effected through bilateral chief centres in the medulla, with subsidiary centres in the spinal cord. Rhythmic stimuli travel from these centres by various nerve paths

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to the diaphragm, intercostal muscles, glottis, etc., to bring about the synchronized acts of inspiration and expiration. These are automatic in their action, but are influenced by voluntary control. The nerve centres are also affected reflexly by afferent impulses from the pharynx and lungs through the vagi nerves, and from the skin surface generally. In addition, the centres are very sensitive to alteration in the chemical composition of the blood, such as variations in its CO_2 and O_2 contents, and to the presence of certain respiratory poisons.

It will be apparent, therefore, that hiccup may be caused directly or reflexly by a great variety of factors, which for purposes of study we may group as follows:—

1. Reflex:
 - (a) affections of the thoracic viscera.
 - (b) " " " abdominal viscera.
 - (c) " " " central nervous system.
2. Epidemic.
3. Neurotic and unknown.
4. Infectious and toxic.

We will consider in detail the various causes under each heading:—

1. *Reflex (a)*.—Stimulation of the phrenic nerve or its communications from any source in the neck or thorax, *e.g.*, tuberculous glands, tumour of the lung or mediastinum, lung abscess, pleurisy, pericarditis, or aneurysm.

(b) Similarly, from any stimuli arising in the abdominal area. For example, one of the most common causes is indiscretion in diet—the use of highly seasoned, very hot or very cold food, alcoholic beverages, or the resultant rapid distension of the stomach. This latter is probably the cause of the hiccup one so frequently sees in nursing infants. Hiccup of serious import may arise from strangulated hernia, intestinal obstruction, ileus, carcinoma, subphrenic abscess, cirrhosis or inflammation of the liver, amœbic dysentery, intestinal parasites, appendicitis, and peritonitis; it is of fairly common occurrence following operations on the gastro-intestinal tract, more particularly those involving the upper abdomen, or where there is much manipulation of the viscera. Hiccup ensuing early, usually from the first to the third day, does not carry with it the grave prognosis of hiccup arising later, which is usually significant of peritonitis, ileus or pneumonia.

(c) From stimuli arising in the central nervous system, particularly from brain tumour

or abscess, hydrocephalus, epilepsy, meningitis, cerebrospinal or tuberculous, tabetic crises, brain injury, cerebral hæmorrhage, and epidemic encephalitis. The hiccup which one occasionally sees during anæsthesia is probably also of central origin. One finds no reference to it in the literature, but it may occur at any stage of anæsthesia, is more common during the administration of ether, and cannot be abolished by the use of carbon dioxide or by increasing the depth of the anæsthetic. It is usually very troublesome to the anæsthetist, but is, fortunately, nearly always, self-limited.

2. *Epidemic*.—Hiccup in epidemic form is described by Rosenow⁴ who considers it to be a variation of encephalitis lethargica. He was unable to demonstrate any lesion in the phrenic or vagus nerves, but found changes in the brain and spinal cord suggestive of encephalitis. He was able to reproduce the condition in animals with naso-pharyngeal washings from infected cases.

3. *Neurotic and unknown*.—Into this group fall those cases of hiccup in hysterical and neurotic patients which are recurrent, of long duration, and intractable under ordinary treatment. The attacks are often excited by worry, anxiety, fear, or sudden shock in those of suitable temperament. Many cases after exhaustive investigation cannot be ascribed to any known cause.

4. *Infectious and toxic*.—Hiccup is found to occur at times in pneumonia, typhoid, cholera, septicæmia, acute rheumatic fever, chronic nephritis, uræmia and diabetes. During influenza epidemics hiccup is frequently seen, either early in the disease or later during convalescence, and does not appear to bear any particular significance. Mayo,⁵ in his recent excellent article on hiccup is convinced of its infectious origin, at least in post-operative cases. He believes in a specific organism, and with Rosenow, he made throat swabs and isolated a streptococcus (*Streptococcus singultus*) which was found to produce diaphragmatic spasm in animals. Men only are affected, usually those over forty-five years of age, and there is a seasonal increase in incidence between November and April. From the number of cases arising after urinary infection or catheterization, he feels that the primary focus is in the prostate.

THE TREATMENT OF HICCUP

In applying treatment, one must consider the probable etiology of the disease. Those cases due to no serious underlying conditions yield fairly readily to a great variety of remedies, popular and scientific. When these fail and when the patient is seriously ill hiccup becomes one of the most difficult and distressing symptoms with which we have to deal, and at times all remedies fail.

In cases of upper respiratory infection Hart and Matheson⁶ report excellent results from spraying the throat with a 2 per cent solution of cocaine, and then applying a 20 per cent solution to the larynx; warm albolene is then slowly dropped into the trachea. Local application to the nasopharynx of menthol or cocaine may also be effectual. Where hiccup is caused by constant direct or reflex stimulation of the phrenic nerve in such cases as mediastinal new growth, diaphragmatic pleurisy, or in reflex stimulation of the nerve from whatever source, the only therapeutic measures of any avail are those which depress the sensitivity of the nerve endings or central nervous system to such a point that conduction is interrupted, or the actual crushing or severing of the phrenic nerve itself. The following drugs should be tried, usually in maximal therapeutic doses,—atropine, luminal, nembutal, bromides, chloral, hyoscine, morphine and its compounds, heroin, nitroglycerin and quinine. The use of sodium amytal intravenously has recently been reported, and the writer has had favourable experience with its administration in prolonged hiccup. A dose of from seven to ten grains is given intravenously, or until the patient becomes unconscious during its administration. Its effect is immediate and usually lasts from two to six hours, when it may be repeated. On account of its tendency to produce pharyngeal paralysis the patient must be constantly, under observation.

Where hiccup arises from the gastrointestinal tract, as is most frequently the case in its simpler forms, removal of the cause is indicated wherever possible. The induction of vomiting often suffices, but, if not, gastric lavage with alkalis should be a routine procedure. Particularly is this true of post-operative hiccup arising early. Following lavage various stomachics or anodynes may be used, such as *Tr. Capsici*, *Tr. Belladonnæ*, *Tr. Moschi*, Hoffman's Anodyne, Chlor-

etone, Benzyl benzoate, Ginger, Peppermint, Chloroform, old brandy, Absinthe, Catnip.⁷ *Carbo Medicinalis*, by virtue of its detoxicating properties, may be tried, particularly in those cases arising post-operatively where partial ileus with toxic absorption may be present. The writer also recommends its use in post-operative vomiting.

There are many simpler expedients which may be effectual in certain cases. Among them are—Valsalva's experiment (attempting to expire forcibly with the glottis closed), sipping ice-water or hot water, traction on the tongue, assuming various bodily contortions, an ice bag, mustard paste, or spraying ethyl chloride on the back of the neck, along the course of the phrenic nerves, or over the area of the insertion of the diaphragm. Blistering of these areas was recommended as early as 1833 by Dr. Shortt,⁸ of Edinburgh. Galvanic stimulation may also be used as described in 1897 by Régis and Debedat.⁹ The inhalation of ammonia or amyl nitrite is sometimes effectual, and finally pressure on the eyeballs or over the carotid sheath on either side. This latter procedure was described in 1885 by Grognot¹⁰ and in 1892 by Leloir.¹¹

There are many advocates of the use of CO₂, alternating with O₂, which acts by interrupting the respiratory rhythm. Jeffery¹² reports a case of nine days' duration, arising post-operatively and complicated by nephritis, where relief was secured by the administration with a gas machine of a mixture of 30 per cent CO₂ and 70 per cent O₂. The effect was transient, however, and repeated administration was necessary. Sheldon,¹³ using varying percentages of CO₂ and O₂, reported similar results. Golden,¹⁴ by utilizing a process whereby the patient re-breathed his own expired air, reported success in a case of short duration only. In my experience this method of treatment should be given a trial but is not the panacea it has been claimed to be.

In the infectious type of hiccup, as described by Mayo and Rosenow, these workers prepared an antibody globulin solution which was used in those cases in which they isolated a specific organism, with apparently dramatic results. Their procedure was as follows. After an initial desensitizing dose, 2 to 5 c.c. were injected intramuscularly two or three times daily. In several cases reported one dose was found to

be efficacious in controlling the symptoms. This serum is apparently not available for general use at present.

In those cases of hiccup which do not yield to any definite treatment, or which persistently recur, or are of long duration, or which, *per se*, are endangering the life of the patient, surgery of the phrenic nerve may be resorted to. As early as 1917 Kroh¹⁵ reported the successful treatment by novocaine injection in ten severe cases. Similar results have been recorded by various workers over the past fifteen years, notably Goetze¹⁶ in 1920, and Ghose.¹⁷ Freezing of the exposed phrenic nerve was later reported on by Kroh,¹⁸ and traction on the nerve by Steinke¹⁹ in 1930. In 1921 Kroh first reported the section of the phrenic nerve for persistent hiccup. Several cases where this treatment was unsuccessful are recorded and are probably explained by the presence of an accessory nerve. In recent years surgery of the phrenic nerve in the treatment of pulmonary tuberculosis has become increasingly common and a technique developed which in skilled hands causes little danger to the patient. I feel that a note of caution should here be introduced, because when surgery is resorted to the patient's condition is often critical, and any undue manipulation or shock may defeat the purpose of the operation. The technique of surgery of the phrenic nerve in intractable hiccup is very thoroughly dealt with by Carnes Weekes²⁰ and Alexander.³ The former quotes a case report where, following perforation of a duodenal ulcer, the patient developed hiccup which persisted for eleven days in spite of all medical treatment. The left phrenic nerve was crushed with complete relief. Five weeks later the patient developed pneumonia and hiccup returned. Two c.c. of a 1 per cent solution of novocaine were then injected into the right phrenic nerve, which was exposed in its course over the scalenus anticus. Hiccup ceased at once, but returned in eight hours. Traction on the nerve caused but temporary cessation, and finally the nerve was crushed with complete relief. In resorting to surgery one must also bear in mind the wisdom

of paralyzing the diaphragm in cases of hiccup where pleurisy or pneumonia are present, or where pneumonia may ensue, for one must realize that by its action it is chiefly responsible for the aeration of the lung bases.

SUMMARY

1. A brief review of the anatomy and physiology of respiration is presented.
2. A classification of hiccup is given, based on its etiology.
3. The various therapeutic agents at our disposal are considered in detail, with particular reference to the use of intravenous sodium amytal, Mayo's antibody globulin solution, Carbo Medicinalis, and surgery involving the phrenic nerve.
4. Caution is urged in the application of surgery on account of the potential risk of hypostatic congestion following paralysis of the diaphragm.

REFERENCES

1. RIDDELL, W. R.: Hippocrates and hiccup, *Med. J. & Rec.*, 1930, 132: 40.
2. GRAY, H.: Anatomy, descriptive and applied, Longmans, Lond., 23rd ed., 1926, p. 952.
3. ALEXANDER, J.: The surgery of pulmonary tuberculosis, Lea & Febiger, Phila., 1925, p. 176.
4. ROSENOW, E. C.: Further studies on etiology of epidemic hiccup and its relation to encephalitis, *Arch. Neurol. & Psychiat.*, 1926, 15: 712.
5. MAYO, C. W.: Hiccup, *Surg., Gyn. & Obst.*, 1932, 55: 700.
6. HART, V. K. AND MATHESON, J. P.: Upper respiratory therapy in persistent hiccough, *Laryngoscope*, 1929, 39: 588.
7. LÉCLERC, H.: La cataire ou herb au chat, *Presse Méd.*, 1928, 36: 1020.
8. SHORTT, T.: Hiccup, its causes and cure, *Edinb. M. & S. J.*, 1833, 39: 305.
9. RÉGIS, E. AND DEBEDAT, X.: Hoquet et éructations hystériques datant de dix mois, etc., *Arch. d'électric-méd.*, 1896, 4: 321.
10. GROGNOT: Traitement du hoquet par la compression des nerfs phrenique et pneumogastrique, *Bull. Gen. de Therap.*, 1885, 108: 253.
11. LÉLOIR, H.: Inhibition du hoquet par un pression sur le nerf phrenique, *Compt. Rend. Acad. de Sc.*, 1892, 114: 138.
12. JEFFREY, S. L.: Carbon dioxide for relief of hiccough, *South. M. J.*, 1931, 24: 406.
13. SHELDON, R. F.: Carbon dioxide in hiccough, *Anaest. & Anal.*, 1927, 6: 31.
14. GOLDEN, L. A.: Control of hiccough with carbon dioxide, *New Eng. J. Med.*, 1931, 204: 1183.
15. KROH, F.: (quoted by Kremer, H.), *Ergebn. der Chir. u. Orthop.*, 1922, 15: 362.
16. GOETZE, O.: Temporary blocking of phrenic nerve, *Zentralbl. f. Chir.*, 1920, 47: 1290.
17. GHOSE, D. M.: Persistent hiccough treated successfully by injections of novocaine into phrenic nerve, *Indian M. Gaz.*, 1926, 61: 124.
18. KROH, F.: Induced paralysis of the diaphragm, *Münch. med. Wchnschr.*, 1922, 69: 807.
19. STEINKE, C. R.: Phrenic nerve surgery, *Ann. Surg.*, 1930, 91: 210.
20. WEEKES, C.: Surgery of phrenic nerve in treatment of intractable hiccup, *Ann. Surg.*, 1931, 93: 811.